

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
Before the Board of Patent Appeals and Interferences

In re Patent Application of
NIKLASON et al
Serial No. 10/074,250
Filed: February 14, 2002
Title: THERAPY FOR CEREBRAL VASOSPASM



Atty Dkt. MJW-01579-0637
C# M#
TC/A.U.: 1617
Examiner: Chong, Y.S.
Date: May 8, 2007

CE
JF

Mail Stop Appeal Brief - Patents

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Correspondence Address Indication Form Attached.

NOTICE OF APPEAL

Applicant hereby **appeals** to the Board of Patent Appeals and Interferences
from the last decision of the Examiner twice/finally rejecting \$500.00 (1401)/\$250.00 (2401) \$
applicant's claim(s).

An appeal **BRIEF** is attached in the pending appeal of the
above-identified application

\$500.00 (1402)/\$250.00 (2402) \$

Credit for fees paid in prior appeal without decision on merits

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A reply brief is attached.

(no fee)

Petition is hereby made to extend the current due date so as to cover the filing date of this
paper and attachment(s)

One Month Extension \$120.00 (1251)/\$60.00 (2251)

Two Month Extensions \$450.00 (1252)/\$225.00 (2252)

Three Month Extensions \$1020.00 (1253)/\$510.00 (2253)

Four Month Extensions \$1590.00 (1254)/\$795.00 (2254) \$

"Small entity" statement attached.

Less month extension previously paid on

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TOTAL FEE ENCLOSED \$ 0.00

Any future submission requiring an extension of time is hereby stated to include a petition for such time extension.
The Commissioner is hereby authorized to charge any deficiency, or credit any overpayment, in the fee(s) filed, or
asserted to be filed, or which should have been filed herewith (or with any paper hereafter filed in this application by this
firm) to our **Account No. 14-1140**. A duplicate copy of this sheet is attached.

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NIXON & VANDERHYE P.C.
By Atty: Mary J. Wilson, Reg. No. 32,955

Signature: Mary J. Wilson



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REPLY BRIEF

In the Examiner's Answer dated March 8, 2007, the Examiner maintains the rejection of claims 1, 10 and 11 under 35 USC 102(b) as allegedly being anticipated by Black (USP 5,527,778). Reversal of the rejection is again requested for the reasons that follow.

The present invention (as claimed in claim 1) relates to a method of treating or inhibiting progression of cerebral vasospasm that follows subarachoid hemorrhage (SAH). The method comprises administering to a patient in need of such treatment or inhibition an amount of an agent that inhibits vascular cell proliferation sufficient to effect the treatment or inhibition. Claim 10 (which depends from claim 1) requires that the agent be a chemotherapeutic agent, and claim 11 (which depends from claim 10)

requires that the chemotherapeutic agent be bis(chloroethyl)nitrosourea, methotrexate or 5-fluorouracil.

Black relates to "a method for selectively opening abnormal brain tissue capillaries ... to allow selective passage of ... neuropharmaceutical agents into the abnormal tissue" (see column 3, line 65 to column 4, line 2). That is, Black describes a method to induce permeability, or "leakiness", in abnormal brain capillaries. The induced "leakiness" allows the selective passage of therapeutic molecules (neuropharmaceutical agents) into the surrounding brain tissue.

Thus, the clinical problem addressed by Black is the "passage of drugs into the abnormal brain tissue". Black provides a method to increase the permeability of the "abnormal brain tissue capillaries", such that drugs can pass through the wall of the capillaries and into the brain tissue. In Black, abnormal brain tissue capillaries are "opened" by infusing bradykinin or a bradykinin analog into the carotid artery of the mammal in an amount sufficient to selectively open the abnormal brain tissue capillaries to allow passage of neuropharmaceutical agents into the abnormal brain tissue without opening the normal brain capillaries to passage of the neuropharmaceutical agent (see column 4, lines 10-18). The method is indicated to be applicable to the treatment of brain tumors, abnormal tissues resulting from multiple sclerosis, ischemia and cerebral abscess. The method is also indicated to be applicable to brain tissue that is inflamed, infected or degenerated due to any number of different diseases. Examples of specific types of abnormal brain tissue are indicated to include, in addition to SAH, gliomas,

metastatic brain tumors, head injury, meningitis, brain abscess and multiple sclerosis (see column 4, lines 2-9).

In the paragraph bridging columns 4 and 5 of Black, it is stated that any of the well known neuropharmaceutical agents can be administered in accordance with the invention (low molecular weight as well as high molecular weight neuropharmaceutical agents). It is also indicated that diagnostic agents can be used including imaging or contrast agents (e.g., substances that are radioactively labelled such as 99-Tc glucoheptonate, gallium-EDTA, ferrous magnetic or iodinated contrast agents). Exemplary neuropharmaceutical agents are indicated to include antibiotics, adrenergic agents, anticonvulsants, nucleotide analogs, chemotherapeutic agents, anti-trauma agents and other classes of agents used to treat or prevent neurological disorders. Black states that specific neuropharmaceutical agents that can be administered into abnormal brain tissue in accordance with the invention include cisplatin, carboplatin, TNF- α , methotrexate, 5-FU, amphotericin, immunotoxins, boron compounds, monoclonal antibodies and cytokines, such as interferons, interleukins, transforming growth factors, oligonucleotides.

Black does not teach that any or all of the above neuropharmaceutical agents can be used to treat any or all of the abnormal brain tissues referenced above. The point made in Black is that infusion of bradykinin or a bradykinin analog in accordance with the method taught by Black allows passage of whatever neuropharmaceutical agent might be necessary to treat the abnormal tissue – e.g., passage of a chemotherapeutic agent to treat a glioma or metastatic brain tumor or passage of an antibiotic to treat brain tissue that is infected.

The Examiner states that:

Black clearly teaches a method of treating abnormal brain tissue, such as SAH, by administering well-known neuropharmaceutical agents, such as methotrexate.

Conspicuous by its absence is any indication by the Examiner as to where that teaching is found. In fact, nowhere in Black is there any such teaching.

Black does not teach, nor would it have suggested, use of a chemotherapeutic to treat anything other than tumors, just as Black does not teach, nor would it have suggested, use of an antibiotic to treat anything other than an infection.

The Examiner contends that Appellants attempted to differentiate the patient population by arguing that the claimed invention relates to arteries not capillaries. Respectfully, the Examiner misses the point. Black teaches treating abnormal brain tissue by selectively opening abnormal brain tissue capillaries in order to allow selective passage of neuropharmaceutical agents to the abnormal brain tissue. The present invention does not relate to the treatment of SAH, as the Examiner contends, but, rather, to the treatment or inhibition of progression of cerebral vasospasm that follows SAH. Cerebral vasospasm is a disease of small- to mid-sized arteries.

The claimed method, in contrast to Black, has nothing to do with capillaries, or with inducing permeability within capillaries, or with delivering drugs to injured brain tissue. Likewise, Black is unrelated to inhibiting cerebral vasospasm that follows.

In the paragraph bridging pages 4 and 5 of the Answer, the Examiner appears to be suggesting that Black inherently teaches treating SAH with a chemotherapeutic. As detailed above, Black includes no such teaching, inherently or otherwise.

At the top of page 5 of the Answer, the Examiner makes reference to an "admission" by Appellant on page 16 of the Appeal Brief. The comment to which the Examiner refers is merely an acknowledgement of the statement that appears in Black at column 4, lines 6-9, nothing more.

At page 5 of the Answer, the Examiner makes reference to Appellants' recitation of "a new mechanism of action for the prior art method" and, again, alludes to some inherent teaching in Black. The claimed invention is fundamentally different from Black and any assertion by the Examiner that Black teaches the use of a chemotherapeutic to treat or inhibit the progression of cerebral vasospasm that follows SAH is totally without merit.

Reversal of the rejection is again requested.

Respectfully submitted,

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